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The funded research has had as its primary goal the identification of the computational significance of key neurobiological characteristics found in a number of telencephalic brain regions. Recent findings have identified novel, computationally valuable algorithms derived from simulation and analysis of specific brain networks, including the olfactory system and the hippocampus as well as auditory neocortex. Analysis has shown that, as might be expected from networks faced with demanding signal-processing tasks under limited-resource situations, these brain-based algorithms have very efficient time and space complexity characteristics and are directly applicable to signal processing tasks of known difficulty, including processing of complex time-varying signals such as speech and sonar.

*Brain learning rules.* The notion that learning arises from synaptic change dates back to suggestions at the turn of the century. To the extent that a synaptic plasticity mechanism is proposed as the substrate for a specific form of learning, it is of significant interest to identify ways in which the characteristics of the plasticity affect the characteristics of the memories arising from it. Studies of the induction and expression of synaptic plasticity, combined with analyses of the anatomical networks within which these synapses are sited, can generate hypotheses about the functional roles that these networks may play in known forms of development and learning (Bear *et al.*, 1987; Miller *et al.*, 1989), to predict network physiological properties (Freeman, 1991), and sometimes previously unanticipated behavioral and memorial properties (Ambros-Ingerson *et al.*, 1990; Granger *et al.*, Submitted). The identification of different forms of plasticity in different brain circuitries suggests that these distinct mechanisms may subserve distinguishable forms of memory. Examples are provided by two major synaptic links inside hippocampus: the mossy-fiber connections from dentate gyrus to field CA3, and the Schaffer-commissural pathway from CA3 to CA1. High-frequency stimulation of either set of fibers results in an enhancement or potentiation of the stimulated synapses. Recent studies have led to the unexpected conclusion that the two forms of potentiation are quite distinct from each other: brief episodes of physiologically-realistic stimulation in the Schaffer fibers elicits synaptic long-term potentiation (LTP) that persists without detectable change for weeks (Staubli and Lynch, 1987). In contrast, mossy fiber potentiation (MFP) is not long-lasting (decrementing over the course of hours), and exhibits few if any of the same chemistries as LTP. MFP, unlike LTP, changes the presynaptic frequency-facilitation characteristics of the synapses, does not require postsynaptic NMDA-receptor stimulation for induction, and may not be synapse-specific (Zalutsky and Nicoll, 1990; Staubli *et al.*, 1990). The existence of different time courses, specificity, and other distinctions between MFP and LTP have led to the suggestion that these two forms of plasticity may underlie memories of different type and duration (Lynch and Granger, 1991; Lynch and Granger, 1992).

*Research progress.* Prominent biological properties of brain networks studied include:

- Physiological characteristics of induction and expression of synaptic long-term potentiation (LTP),
- Rhythms and temporal patterns exhibited during learning and memory behavior and their relationships to biological events,
- Anatomical characteristics of specific architectures in different regions,
- Distinct dendritic architectures of cells comprising these regions.

Progress in this research program has led to (i) neurobiologically based hypotheses about the types of memory operations carried out by specific brain regions and thus their contributions to behavioral memory, and (ii) useful computational algorithms and possibly devices derived from these identified operations. These results stand in contrast to the very real possibility that many of the detailed characteristics of neural circuitry might turn out to be superfluous to the computational tasks carried out by that circuitry. It might have been the case, for the olfactory/hippocampal systems we have studied, that sparse anatomical connectivity, repetitive activation at the fixed theta rhythm, the relative longevity of inhibitory versus excitatory postsynaptic potentials, the differential range of spiking threholds for olfactory mitral bulb cells, and feedback from layer III paleocortical pyramidal neurons to inhibitory bulb granule cells, to name a few examples, would have useful biological properties but no important computational ones. For the five examples just cited, this has turned out not to be the case: specific computational benefits of each of these anatomical and physiological features have been identified, leading to published findings (Granger *et al.*, 1989; Ambros-Ingerson *et al.*, 1990; Coultrip *et al.*, 1992; Antón *et al.*, 1991).

The bulk of our neurobiological research has centered on the synaptic LTP effect, and in particular on the relationship of its induction characteristics to physiological cell firing patterns that occur during learning behavior. Our modeling efforts have focussed on the olfactory-hippocampal pathway, representing a sequence of telencephalic circuits extending from the olfactory periphery into central brain structures implicated in learning and memory. This program of research elucidated a candidate hypothesis of memory storage and retrieval operations in the olfactory portion (bulb and cortex) of the olfactory-hippocampal system, consisting of spatial and temporal codes and responses synchronized to the theta rhythm, resulting in sequential hierarchical encoding of perceptual cues (Granger *et al.*, 1989; Ambros-Ingerson *et al.*, 1990). Behavioral correlates of this hypothesis have been investigated (Granger *et al.*, 1991) and physiological predictions have been tested in behaving animals (McCollum *et al.*, 1991).

*Graduate and undergraduate training.* The collaboration in this grant between computer scientist Richard Granger and neurobiologist Gary Lynch offered a unique opportunity for graduate student training in cross-disciplinary pursuits focusing on the computational analysis of brain circuitry:

- Most of the grant funding was used for support of graduate student researchers;
- New courses have been created and taught at the graduate and undergraduate levels, crossing traditional disciplinary boundaries and training students in depth in computational neuroscience;
- Graduate student researchers are co-authors on many of the articles published by this collaborative research group;
- Many graduate students have received their Ph.D.s in computer science or psychobiology specializing in computational neuroscience based on the training received in classes offered by the faculty in this group (Lynch and Granger) combined with individual in-depth research experience in these collaborative laboratories.

*Summary of published findings.* This grant funded collaborative efforts comprising a coherent program of research incorporating biophysical modeling of individual cells, local-circuit modeling of small groups of ($\sim$ 100) cells, network modeling of entire circuits and systems modeling of circuit interactions. Results of these investigations included the successful construction of a number of models of circuits comprising the olfactory-hippocampal pathway, and concomitant tests and applications.

1. a model of the normalization of bulb activity via dendrodendritic interactions among mitral and granule cells (Antón *et al.*, 1991; Anton *et al.*, 1992; Antón *et al.*, 1993);
2. incorporation of these and temporal LTP learning rules into our olfactory bulb-cortex model (Granger and Lynch, 1991; Coultrip *et al.*, 1992; Gluck and Granger, 1993; Granger and Lynch, 1991);
3. construction of a model of hippocampal field CA1 (Granger *et al.*, Submitted); construction of a combined olfactory-CA1 model (Granger and Lynch, 1993);
4. testing of the combined model on static sonar and speech data (Granger *et al.*, 1993; Speidel *et al.*, 1993);
5. construction of a model of hippocampal field CA3 (Taketani *et al.*, 1992);
6. construction of a combined olfactory-CA3-CA1 model (Lynch and Granger, 1992);
7. testing of the combined model on sample continuous speech data.

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